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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/423,126	11/05/99	BUCHTER-LARSEN	A 674509-2020

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HM12/1009

EXAMINER	
SOUAYA, I	
ART UNIT	**PAPER NUMBER**
1655	12

DATE MAILED: 10/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/423,126	Buchter-Larsen et al
Examiner	**Art Unit**
Jehanne Souaya	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Jul 20, 2001*.

2a)☒ This action is **FINAL.** 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some* c)☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18)☐ Interview Summary (PTO-413) Paper No(s). _____
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

1. Currently, claims 1-25 are pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied (necessitated by amendment) or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

3. Applicant's election with traverse of Group I in Paper No. 11 is acknowledged. The traversal is on the ground(s) that 1) the amino acid sequences of SEQ ID NOS 1-6 and the nucleic acid sequences encoding them, SEQ ID NOS 7-12 are drawn functionally to the same enzyme, a glucan lyase, and 2) that a search of all of the related nucleotide and amino acid sequences presented in the application does not pose a serious burden on the office. These arguments have been thoroughly reviewed but were found unpersuasive. Firstly, the amino acid sequences of the glucan lyases of SEQ ID NOS 1-6 are to different amino acid sequences that do not appear to be obvious variants of each other. These amino acid sequences are structurally different from each other. Secondly, the search of these sequences does pose a serious burden to the office and to the examiner as the database search required for all 6 glucan lyases is extremely time consuming,

especially given the large numbers of sequences now present in the databases. For these reasons, and the reasons made of record in the previous office action, the requirement is still deemed proper.

Claim Rejections - 35 USC § 112

Written Description

4. Claims 1-6, 8, and 10-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a process for producing any anti-oxidant in any medium which comprises a component which is any plant (which could be a cereal or a fruit, such as a grape) or part thereof, wherein any recombinant enzyme (which may be a glucan lyase such as the amino acid of SEQ ID NO 1, or any variant, homologue or fragment thereof) is expressed in the plant or part thereof and acts on any glucan substrate which is present either in the medium and the component or in the component only to produce any anti-oxidant (which may be 1,5-D-anhydrofructose). The specification teaches that the invention provides a method of preparing *in situ* in an oxidizable medium an anti-oxidant. The specification teaches the amino acid sequence of 6 glucan lyases (SEQ ID NOS 1-6) which could be suitable for producing 1,5-D-anhydrofructose from starch (p.11).

With regard to the broadest interpretation of the claim, the specification, however, fails to teach the method of the claimed invention with regard to any recombinant enzyme expressed in any plant to produce any anti-oxidant from a glycan. Regarding the narrower interpretation of the claims to a specific glucan lyase such as SEQ ID NO1 or any variant, homologue, or fragment thereof, the specification only teaches 6 different glucan lyases. The specification does not teach variants or homologs or fragments of such glucan lyases, nor does the specification teach converting a glucan to anhydrofructose using any variant, homolog or fragment of proteins having SEQ ID NOS 1-6 as taught in the specification. Furthermore, the specification only presents the amino acid sequences in SEQ ID NOS 1-6 of the 6 possible glucan lyases, but does not teach their relationship to each other, ie are they homologs or variants of one another? The specification only references WO publications where these glucan lyases can be found but does not appear to incorporate them by reference into the specification. Therefore the specification fails to teach how these glucan lyases are related to each other, let alone their ability to be expressed in plants to produce anhydrofructose from a glucan.

Additionally, although the specification teaches how to transform a plant such as maize or grape or potatoes with a glucan lyase, the specification does not teach having done so, nor does the specification teach having produced an anti-oxidant such as anhydrofructose from a glucan where the glucan is present in either the medium and the plant, or the plant only, using the methods taught in the specification. As set forth by the Court in *Vas Cath Inc. V. Mahurkar,* 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable

clarity" that as of the filing date, applicant was in possession of the claimed invention. The specification teaches possession of the proteins of SEQ ID NOS 1-6, however the specification has not shown with reasonable clarity any variant, homolog or fragment of such sequences. Furthermore, the specification has not shown with reasonable clarity the production of any anti-oxidant in any medium which comprises a component which is any plant or part thereof, wherein any recombinant enzyme is expressed in the plant or part thereof and acts on any glucan substrate which is present either in the medium and the component or in the component only to produce any anti-oxidant. Although the specification teaches how to transform a plant such as maize or grape or potatoes with a glucan lyase, the specification does not teach having done so, nor does the specification teach having produced anhydrofructose from a glucan that is present in the medium and the plant or in the plant itself wherein the glucan lyase is expressed in the plant. Each of the claimed invention is a broad genus for which a representative number of species for each genus must be disclosed to meet the written description requirement of 112 first paragraph. Absent such a written description, the specification fails to show that applicant was "in possession of the claimed invention" at the time the application for patent was filed.

Response to Arguments

The response traverses that the instant invention is clearly enabled because a skilled artisan would readily understand how to make and use the invention. This argument was fully considered. The examiner agrees with applicants assertion and respectfully points out that the

rejection under 35 USC 112, first paragraph was made with regard to written description and to with regard to enablement. The prior art teaches glucan lyases, how to transform organisms to express glucan lyases and further teaches how to transform plants through genetic engineering. The examiner has withdrawn the written description rejection with regard to claims 7 and 9 as the specification teaches the exact sequences of SEQ ID NOS 1 and 7, however the remaining claims broadly encompass expressing any enzyme [as well as any glucan lyases], that "act" on a glucan, from any source. As set forth by the Court in *Vas Cath Inc. V. Mahurkar,* 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date, applicant was in possession of the claimed invention. The specification teaches possession of the glucan lyases of SEQ ID NOS 1-6, however the specification has not shown with reasonable clarity any variant, homolog or fragment of such sequences, from any source. Furthermore, the specification has not shown with reasonable clarity the production of any anti-oxidant in any medium which comprises a component which is any plant or part thereof, wherein any recombinant enzyme is expressed in the plant or part thereof and acts on any glucan substrate which is present either in the medium and the component or in the component only to produce any anti-oxidant.

Claim Rejections - 35 USC § 103

5. Claims 1-18 and amended claim 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al (US Patent 6,013,504, 102(e) date: 7/2/1996, hereinafter referred to as

Yu(a)) or in the alternative, Yu et al (WO 95/10618, international publication date: April 20, 1995, hereinafter referred to as Yu(b)) in view of Poulsen (WO 97/04113) and Ishida et al (Nature Biotechnology, vol. 14, 1996, pp 745-750) and Perl et al (Nature Biotechnology, vol.14, 1996, pp 624-628).

The claims are broadly drawn to a process for producing any anti-oxidant in any medium which comprises a component which is any plant or part thereof, wherein any recombinant enzyme is expressed in the plant or part thereof and acts on any glucan substrate which is present either in the medium and the component or in the component only to produce any anti-oxidant. The claims are more narrowly drawn to producing 1,5-D-anhydrofructose in a medium wherein a glucan lyase such as the amino acid of SEQ ID NO 1, or any variant, homologue or fragment thereof is expressed in component of the medium which could be a cereal or a fruit, such as a grape. Both Yu(a) and Yu (b) teach the nucleic acid and amino acid sequences of glucan lyases that can convert α 1,4 glucan lyase to 1,5-D-anhydrofructose (Yu (a) see abstract, col 4, SEQ ID NOS 3 and 4, [SEQ ID NO 3 is identical to SEQ ID NO 1 of the instantly claimed invention]; Yu(b) abstract, p.p. 17, 19, SEQ ID NOS 1-4, [SEQ ID NO 3 is identical to the instantly claimed SEQ ID NO 1]). Yu (a) and Yu (b) teach expression of this glucan lyase in microorganisms (Yu (a) see col. 14, Yu (b) see p 23) and teach that lyase activity (production of anhydrofructose) was observed in the medium with both *Pichia pastoris* and *Aspergillus niger* (see col. 14 of Yu(a) and p. 27 of Yu(b)). Yu (a) and Yu(b) further teach that these results indicate that active lyase was secreted from the cells and that the lyase activity was also measured in cell free extract (Yu (a)

col. 15, Yu (b) p. 27-27). Yu (a) and Yu(b) also teach that instead of Aspergillus niger as host, preferred embodiments include any transformed host organism having the capability of producing AF as a consequence of the introduction of a DNA sequence, and further teach contemplating a method for preparing 1,5-D-anhydrofructose by contacting α 1,4 glucan with α 1,4 glucan lyase expressed in a transformed host organism by transforming the host organism with a nucleic acid described in Yu (a) and Yu (b) (Yu (a) see col. 16, lines 25-30 and 37-40; Yu (b) see p. 29).

Although neither Yu (a) nor Yu(b) teach transforming a plant with SEQ ID NO 1, Yu (a) and Yu(b) provide motivation for the ordinary artisan to do so in contemplating the transformation of any host organism that can produce anhydrofructose. The ordinary artisan would have further been motivated to produce anhydrofructose as Yu (a) teaches that anhydrofructose can be a precursor for the preparation of the antibiotic pyrone microthecin (see col. 1, lines 17-20). As applicants have stated in the instant specification, methods of transforming plants was widely known in the art and was readily practiced at the time of the invention. Poulsen teaches transformation of potatoes (pages 24-28), Ishida teaches transformation of maize, and Perl et al teaches the transformation of grapes. Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the method of Yu (a) or Yu(b) to transform potatoes or maize or grapes to express α 1,4 glucan lyase to produce anhydrofructose, as Yu a &b teach the successful transformation of microorganisms to express α 1,4 glucan lyase and produce anhydrofructose and teach that such a method could be used to transform any host organism capable of producing anhydrofructose. The

ordinary artisan would have considered the transformation of plants to be equivalent host organisms and would have been enabled in a method of transforming a plant to express a glucan lyase as 1)Yu a&b both teach how to transform an organism, ie teach the nucleic acid sequences of glucan lyases that can produce anhydrofructose, and 2) the state of the art was very high at the time the invention was made as to how to successfully transform plants to express an enzyme of interest.

Response to Arguments

The response traverses that neither Yu a or b mention transforming a plant to express α 1,4 glucan lyase and that neither Poulsen, Ishida or Perl provide motivation to the ordinary artisan to do so. The response further traverses that the Office Action has not shown a document which motivates the ordinary artisan to even attempt to express any enzyme, for example α 1,4 glucan lyase, in a plant to produce *in situ* an anti-oxidant, for example AF, from a glucan substrate. This argument has been thoroughly reviewed but was found unpersuasive as it was widely known in the art at the time of the invention that expression of anti-oxidants in plants could be used to improve the stress tolerance of plants (see forthcoming rejection with respect to amended claims 19-25). The references do not have to explicitly suggest combining teachings, see MPEP 2144 below.

2144 Sources of Rationale Supporting a Rejection Under 35 U.S.C. 103
RATIONALE MAY BE IN A REFERENCE, OR REASONED FROM COMMON KNOWLEDGE IN THE ART, SCIENTIFIC PRINCIPLES, ART-RECOGNIZED EQUIVALENTS, OR LEGAL PRECEDENT
The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). See also

In re Eli Lilly & Co., 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990) (discussion of reliance on legal precedent); In re Nilssen, 851 F.2d 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988) (references do not have to explicitly suggest combining teachings); Ex parte Clapp, 227 USPQ 972 (Bd. Pat. App. & Inter. 1985) (examiner must present convincing line of reasoning supporting rejection); and Ex parte Levengood, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993)(reliance on logic and sound scientific reasoning).

New Grounds of Rejection

6. Newly amended claims 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al (US Patent 6,013,504, 102(e) date: 7/2/1996, hereinafter referred to as Yu(a)) or in the alternative, Yu et al (WO 95/10618, international publication date: April 20, 1995, hereinafter referred to as Yu(b)) in view of Poulsen (WO 97/04113) and Ishida et al (Nature Biotechnology, vol. 14, 1996, pp 745-750) and Perl et al (Nature Biotechnology, vol.14, 1996, pp 624-628) as applied to claims 1-18 above, and further in view of Adams et al (US Patent 5,780,709) and Kenne et al (WO 94/09122).

Both Yu(a) and Yu (b) teach the nucleic acid and amino acid sequences of glucan lyases that can convert α 1,4 glucan lyase to 1,5-D-anhydrofructose (Yu (a) see abstract, col 4, SEQ ID NOS 3 and 4, [SEQ ID NO 3 is identical to SEQ ID NO 1 of the instantly claimed invention]; Yu(b) abstract, p.p. 17, 19, SEQ ID NOS 1-4, [SEQ ID NO 3 is identical to the instantly claimed SEQ ID NO 1]). Yu (a) and Yu (b) teach expression of this glucan lyase in microorganisms (Yu (a) see col. 14, Yu (b) see p 23) and teach that lyase activity (production of anhydrofructose) was observed in the medium with both *Pichia pastoris* and *Aspergillus niger* (see col. 14 of Yu(a) and p. 27 of Yu(b)). Yu (a) and Yu(b) further teach that these results indicate that active lyase was secreted from the cells and that the lyase activity was also measured in cell free extract (Yu (a)

col. 15, Yu (b) p. 27-27). Yu (a) and Yu(b) also teach that instead of Aspergillus niger as host, preferred embodiments include any transformed host organism having the capability of producing AF as a consequence of the introduction of a DNA sequence, and further teach contemplating a method for preparing 1,5-D-anhydrofructose by contacting α 1,4 glucan with α 1,4 glucan lyase expressed in a transformed host organism by transforming the host organism with a nucleic acid described in Yu (a) and Yu (b) (Yu (a) see col. 16, lines 25-30 and 37-40; Yu (b) see p. 29). Poulsen teaches transformation of potatoes (pages 24-28), Ishida teaches transformation of maize, and Perl et al teaches the transformation of grapes.

With regard to claims 21, 23 and 25, the claims are drawn to imparting or improving the transformation of a grape comprising administering anhydrofructose wherein the anhydrofructose is produced *in situ*. Although the combined teachings of Yu a&b and Poulson, Perl, and Ishida do not teach transforming a grape to produce anhydrofructose *in situ*, it would have been prima facie obvious to one of ordinary skill in the art to transform a grape such that it produced anhydrofructose in situ as Perl teaches the stable transformation of grapes and the improvement in plant viability when a mixture of antioxidants was added (see p. 62, cols 1 and 2) during and after cultivation. The ordinary artisan would have been motivated to transform a grape to produce anhydrofructose in situ as it was known at the time of the invention that anhydrofructose was an antioxidant (Kenne et al), the art teaches how to produce anhydrofructose *in situ* by transformation to express a glucan lyase, the art teaches how to transform plants, and Perl

teaches the stable and improved transformation of grapes only after using anti-oxidants during and after cocultivation.

With regard to claims 20, 22, and 24, the claims are drawn to imparting or improving stress tolerance in a plant by administering anhydrofructose wherein the anhydrofructose is produced *in situ*. Although the combined teachings of Yu a&b and Poulson, Perl, and Ishida do not teach transforming a plant to produce anhydrofructose *in situ*, it would have been further *prima facie* obvious to one of ordinary skill in the art to transform a plant such that it produced anhydrofructose *in situ* because Adams teaches that transformed tobacco plants that expressed enzymes that produced antioxidants *in situ* had decreased weight loss and increased height relative to untransformed plants when exposed to high concentrations of NaCl (see col. 2). Adams teaches that of the mechanisms employed by water deficit tolerant plants to grow and yield, those with major impact on plant productivity are osmotic adjustment through the increased synthesis of osmoprotective metabolites, such as sugars, which include fructose (see col. 1, lines 55-60 and col 2, lines 60-67). Adams teaches the successful growth of corn transformed to produce mannitol, another antioxidant. The ordinary artisan would have been motivated to transform a plant to produce anhydrofructose in situ as it was known at the time of the invention that anhydrofructose was an antioxidant (Kenne et al), the art teaches how to produce anhydrofructose *in situ* by transformation of an organism to express a glucan lyase, the art teaches how to transform plants, and Adams teaches that transformed tobacco plants that

expressed enzymes that produced antioxidants *in situ* had decreased weight loss and increased height relative to untransformed plants when exposed to high concentrations of NaCl.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. No claims are allowable over the cited prior art.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Oct. 2, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600